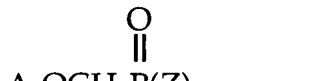
CLAIMS

We claim:

1. A compound having formula (1a)



(1a)

wherein Z is independently $-OC(R^2)_2OC(O)X(R)_a$, an ester, an amidate or -H, but at least one Z is $-OC(R^2)_2OC(O)X(R)_a$;

A is the residue of an antiviral phosphonomethoxy nucleotide analog;

X is N or O;

R^2 independently is -H, C_1-C_{12} alkyl, C_5-C_{12} aryl, C_2-C_{12} alkenyl, C_2-C_{12} alkynyl, C_7-C_{12} alkenylaryl, C_7-C_{12} alkynylaryl, or C_6-C_{12} alkaryl, any one of which is unsubstituted or is substituted with 1 or 2 halo, cyano, azido, nitro or $-OR^3$ in which R^3 is C_1-C_{12} alkyl, C_2-C_{12} alkenyl, C_2-C_{12} alkynyl or C_5-C_{12} aryl;

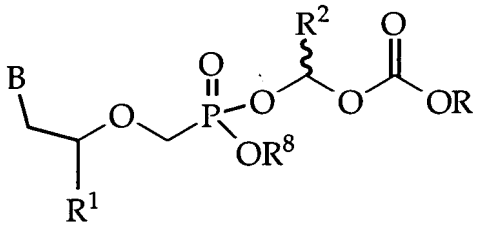
R is independently -H, C_1-C_{12} alkyl, C_5-C_{12} aryl, C_2-C_{12} alkenyl, C_2-C_{12} alkynyl, C_7-C_{12} alkyenylaryl, C_7-C_{12} alkynylaryl, or C_6-C_{12} alkaryl, any one of which is unsubstituted or is substituted with 1 or 2 halo, cyano, azido, nitro, $-N(R^4)_2$ or $-OR^3$, where R^4 independently is -H or C_1-C_8 alkyl, provided that at least one R is not H; and

a is 1 when X is O, or 1 or 2 when X is N;

with the proviso that when a is 2 and X is N, (a) two N-linked R groups can be taken together to form a carbocycle or oxygen-containing heterocycle, (b) one N-linked R additionally can be $-OR^3$ or (c) both N-linked R groups can be -H;

and the salts, hydrates, tautomers and solvates thereof.

2. The compound of claim 1 having formula (1)



(1)

wherein B is guanin-9-yl, adenin-9-yl, 2,6-diaminopurin-9-yl, 2-aminopurin-9-yl or their 1-deaza, 3-deaza, or 8-aza analogs, or B is cytosin-1-yl;

R is independently -H, C_1-C_{12} alkyl, C_5-C_{12} aryl, C_2-C_{12} alkenyl, C_2-C_{12} alkynyl, C_7-C_{12} alkenylaryl, C_7-C_{12} alkynylaryl, or C_6-C_{12} alkaryl, any one of which is unsubstituted or is substituted with 1 or 2 halo, cyano, azido, nitro or -OR^3 in which R^3 is C_1-C_{12} alkyl, C_2-C_{12} alkenyl, C_2-C_{12} alkynyl or C_5-C_{12} aryl;

R^1 is hydrogen, -CH_3, -CH_2OH, -CH_2F, -$CH{=}CH_2$, or -CH_2N_3, or R^1 and R^8 are joined to form -CH_2-;

R^2 independently is hydrogen or C_1-C_6 alkyl; and

R^8 is hydrogen or -CHR^2-O-C(O)-OR, or R^8 is joined with R^1 to form -CH_2-;

and the salts, hydrates, tautomers and solvates thereof.

3. The compound of claim 2 wherein R^2 is -H.

4. The compound of claim 3 wherein R^1 is -CH_3.

5. The compound of claim 1 wherein R^2 is -H.

6. The compound of claim 1 wherein one R^2 is -CH_3 and the other R^2 is H.

7. The compound of claim 1 wherein R^3 is C_1-C_6 alkyl or phenyl.

8. The compound of claim 1 wherein R^3 is -CH_3 or -C_2H_5.

9. The compound of claim 1 wherein X is O.

10. The compound of claim 1 wherein X is N and one R^3 is H.

11. The compound of claim 4 wherein the compound is enriched or resolved at the carbon atom chiral center linked to R^1.

12. The compound of claim 4 wherein at least about 90% of the compound is in the (*R*) configuration at the R^1 site.

13. The compound of claim 12 wherein B is adenin-9-yl.

14. The compound of claim 13 wherein each R is ethyl.

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15. The compound of claim 13 wherein each R is isopropyl.

16. The compound of claim 13 wherein each R is 3-pentyl or neopentyl.

17. The compound of claim 13 wherein each R is *t*-butyl or isobutyl.

18. The compound of claim 4 wherein B is 2,6-diaminopurin-9-yl.

19. The compound of claim 3 wherein R^1 is H.

20. The compound of claim 19 wherein B is adenin-9-yl.

21. The compound of claim 4 wherein R is C_1-C_{12} alkyl.

22. The compound of claim 3 wherein R^1 is -CH_2OH.

23. The compound of claim 22 wherein B is cytosin-1-yl.

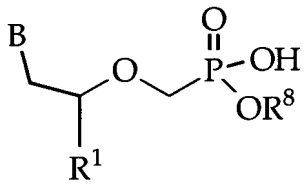
~~24. The compound of claim 1 named in Table B and compound groups 1-19.~~

25. The compound of claim 22 wherein at least about 90% of the compound is in the (*S*) configuration at the R^1 site.

26. A method comprising orally administering to a patient infected with virus or at risk to viral infection a therapeutically effective amount of a compound of claim 1.

27. A method for preparing a compound of formula (1a) of claim 1 comprising reacting the diacid of a phosphonomethoxy nucleotide analog with L-$CH(R^2)OC(O)X(R)_n$ wherein L is a leaving group.

28. A method for preparing a compound of formula (1) of claim 2 comprising reacting a compound of formula (6)



(6)

with L-CHR^2-O-C(O)-OR and recovering a compound of formula (1), wherein B is guanin-9-yl, adenin-9-yl, 2,6-diaminopurin-9-yl, 2-aminopurin-9-yl or their 1-deaza, 3-deaza, or 8-aza analogs, or B is cytosin-1-yl;

R^1 is hydrogen, -CH_3, -CH_2OH, -CH_2F, -$CH{=}CH_2$, -CH_2N_3 or R^1 and R^8 are joined to form -CH_2-; and

R^8 is hydrogen, -CHR^2-O-C(O)-OR or R^8 is joined with R^1 to form -CH_2-; and

R^2 is H, C_1-C_{12} alkyl, aryl, alkenyl, alkynyl, alkyenylaryl, alkynylaryl, alkaryl, arylalkynyl, arylalkenyl or arylalkyl which is unsubstituted or is substituted with halo, azido, nitro or OR^3 in which R^3 is C_1-C12 alkyl;

R is independently H, C_1-C_{12} alkyl, aryl, alkenyl, alkynyl, alkyenylaryl, alkynylaryl, alkaryl, arylalkynyl, arylalkenyl or arylalkyl which is unsubstituted or is substituted with halo, azido, nitro or OR^3, provided that at least one R is not H; and

L is a leaving group.

a 28 27 ~~29.~~ ~~28~~ The method of claim ~~30~~ comprising conducting the reaction using at least about 1.0 equivalent of L-CHR^2-O-C(O)-OR.

a 29 27 ~~30.~~ ~~28~~ The method of claim ~~31~~ comprising conducting the reaction in the presence of an organic base in an organic solvent at a reaction temperature of about 4-100°C for about 4-72 hours.

30 27 ~~31.~~ ~~28~~ The method of claim ~~28~~ wherein the compound of formula (1) is recovered by forming a salt, precipitating the salt and recovering the precipitated salt.

31 30 ~~32.~~ ~~31~~ The method of claim ~~31~~ wherein the salt is formed from sulfuric acid, phosphoric acid, lactic acid, or citric acid.